Synchrony and the Art of Mechanical Ventilation

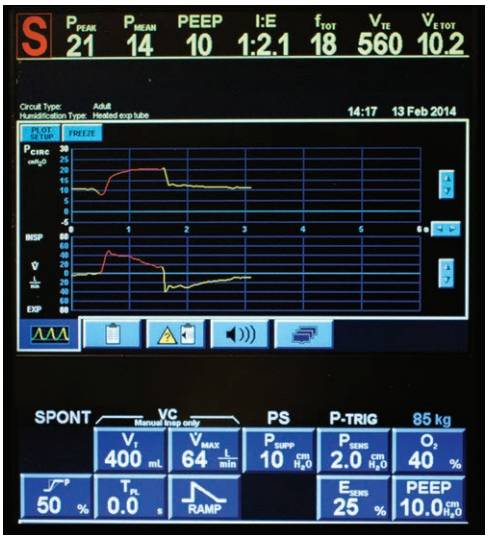
Ewan C. Goligher, M.D., Ph.D.

Life is short,
And art long,
Opportunity fleeting,
Experimentations perilous,
And judgment difficult.

–Hippocrates, *Aphorisms*

"LIFE is short, and art long," wrote Hippocrates in his *Aphorisms*. Only as one begins to develop some mastery in the practice of medicine does one begin to conceive of the complexities of caring for the sick and to acquire the art of managing those complexities. Artistry—even the mere appreciation of it—comes as the clinician matures in practice.

Although Hippocrates was probably not thinking of mechanical ventilation when he wrote *Aphorisms*, his proverb very much applies to this rapidly evolving and critically important technologic intervention in modern medicine. Clinicians managing ventilation must juggle multiple competing concerns: adequate acid–base homeostasis, ventilator-induced lung injury, ventilator-induced diaphragm dysfunction, and sedation-related immobility. Moreover, there is now a burgeoning body of literature on the complex challenge of synchronizing patient and ventilator exemplified by the rigorous and insightful study of Rolland-Debord *et al.*,[1] published in this issue of Anesthesiology. As the field matures, the art of mechanical ventilation has become very complex indeed.



"The art of mechanical ventilation…synchronizing patient and ventilator… has become very complex indeed."

The mechanical ventilator can be conceived of as an adjunctive respiratory muscle. This muscle functions most effectively when its action is coordinated synchronously with the patient's own inspiratory muscles: they should drive inspiratory gas flow simultaneously and passively permit expiratory gas flow simultaneously. The technologic challenges of achieving this synchrony are not insignificant; modern ventilators are exquisitely responsive to changes in flow and pressure within the circuit resulting from patient inspiratory effort. Nevertheless, these mechanical signals of patient respiratory muscle effort are sometimes absent or misinterpreted by the ventilator, resulting in dyssynchrony. The adjunct mechanical respiratory muscle (the ventilator) may fail to "contract" when the patient inspires (ineffective triggering), it may contract without any patient inspiratory effort (autotriggering), it may contract twice during a single patient breath (double triggering), it may continue to contract when the patient attempts to exhale (delayed cycling), or its contraction may stimulate the patient's respiratory muscles to contract in response (reverse triggering).

Dyssynchrony is thus a physiologically complex and varied phenomenon, and real skill and mastery are required to detect and effectively treat dyssynchrony. Such efforts are motivated by a concern for the patient's well-being, and this naturally raises the question as to whether dyssynchrony has any important impact on clinical outcome. Rolland-Debord *et al.* took up this question, focusing on the period when patients transition from controlled ventilation to partially assisted ventilation. They conducted a secondary analysis of a previous randomized controlled trial comparing pressure support ventilation with neurally adjusted ventilatory assist ventilation in patients recovering from acute respiratory failure[2] using two different approaches to ascertain dyssynchrony. They found that the estimated prevalence of dyssynchrony is considerably higher when the diaphragm electrical activity signal is used to detect the patient's inspiratory effort and timing and the rate of dyssynchrony (ascertained by either technique) was not associated with clinical outcomes including duration of ventilation, duration of intensive care unit stay, and risk of death.

The absence of an association between dyssynchrony and outcome in this study is somewhat surprising given other recent studies that found a significant association between dyssynchrony and patient outcomes.[3–5] An association may not be detected for several reasons, including misclassification

Image: J. P. Rathmell.

Corresponding article on page 989.

Accepted for publication September 7, 2017. From the Interdepartmental Division of Critical Care Medicine, University of Toronto, Toronto, Ontario, Canada; and the Division of Respirology, Department of Medicine, University Health Network, Toronto, Ontario, Canada.

Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. All Rights Reserved. Anesthesiology 2017; 127:915-7

Downloaded from anesthesiology.pubs.asahq.org by guest on 04/03/2020
Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.
<zdoi;10.1097/ALN.0000000000001921>

of exposure or outcome, confounding that masks the true effect of exposure on outcome, or because there truly is no effect to be detected. Several issues merit consideration.

First, the challenges of accurately classifying the exposure (dyssynchrony) are highlighted by the extreme variance in the estimates of prevalence between the two methods used by Rolland-Debord *et al.* Using the conventional method of assessing airway pressure and flow tracings, they found that only 7% of patients exhibited severe asynchrony, whereas 86% met criteria for severe asynchrony when using the diaphragm electrical activity signal. In the absence of respiratory muscle tracings (esophageal pressure or diaphragm electrical activity), dyssynchrony is notoriously difficult to detect, even for experts.[6] It is therefore not surprising that reported prevalence was markedly higher when diaphragm electrical activity was considered. Yet the rate of severe asynchrony ascertained based on diaphragm electrical activity seems excessively high and raises questions as to whether the definitions used were overly sensitive such that noise from misclassification might mask a true signal for effect of dyssynchrony on outcome. Interestingly, the frequencies (per minute) of most forms of dyssynchrony were actually relatively low in this study; it may be that the asynchrony index does not always reliably reflect the true burden of dyssynchrony. Moreover, recent work suggests that clinically significant dyssynchrony tends to occur in clusters, making it more difficult to detect without continuous monitoring.[4]

Second, the putative causal pathway from dyssynchrony to patient outcome is complex,[7] and not every form of dyssynchrony is likely to carry the same pathophysiologic significance. Dyssynchrony might delay liberation from ventilation by several mechanisms: ineffective triggering is likely to increase the work of breathing, oxygen consumption, and respiratory distress, leading to increased sedation requirements and possible load-induced diaphragm injury.[8] Double triggering can cause lung injury by preventing complex exhalation of each tidal breath, increasing lung stress.[9] Reverse triggering may increase tidal volume and induce eccentric diaphragm contractions. However, dosage (not merely frequency) is likely key for both of these forms of dyssynchrony. Validated criteria for these forms of dyssynchrony would ideally take into account not only the phenomenology of the event but also the pathophysiologic impact.[9] Efforts to develop validated definitions of dyssynchrony supported by independent physiologic and outcome data—similar to the approach used in the Berlin definition of acute respiratory distress syndrome[10]—may yield clinically relevant estimates of the prevalence of dyssynchrony.

Third, all of the observational studies examining the relationship between dyssynchrony and outcome are at high risk of bias from confounding: patients with dyssynchrony are likely systematically different than those without dyssynchrony. To address this challenge, the case for or against causation could be bolstered by examining the relationship between dyssynchrony and putative causal pathways—lung or diaphragm injury, for example—that are believed to mediate poor patient outcomes. Ultimately, a causal effect of dyssynchrony on patient outcome can only be confirmed or refuted in a randomized trial of an intervention known to reduce dyssynchrony. In fact, Rolland-Debord *et al.* have already conducted a preliminary version of such a trial: in comparison to pressure support ventilation, neurally adjusted ventilatory assist ventilation (which reduces dyssynchrony) was associated with intriguing nonsignificant trends toward improvement in certain patient outcomes[2] (the trial was not powered for those endpoints). Future larger trials could use mediation analysis to evaluate the extent of the role of dyssynchrony in the causal pathway to outcome.

In the end, synchronizing patient and ventilator may be of value, irrespective of any impact (or lack thereof) on outcome. Dyssynchrony might contribute to dyspnea, a prevalent and distressing symptom in mechanically ventilated patients.[12] Relieving such distress is an important patient-centered priority. Detecting dyssynchrony and adjusting ventilation to improve synchrony require astute attention to detail and mastery of the technique of mechanical ventilation. If medicine (and mechanical ventilation) is an art as much as it is a science, then for the artful clinician synchrony is surely an end worth pursuing, however difficult it may be to attain.

Competing Interests

Dr. Goligher's research receives support in the form of equipment from Gëtinge AB (Gothenburg, Sweden) and General Electric (Boston, Massachusetts).

Correspondence

Address correspondence to Dr. Goligher: ewan.goligher@mail.utoronto.ca

References

1. Rolland-Debord C, Bureau C, Poitou T, Belin L, Clavel M, Perbet S, Terzi N, Kouatchet A, Similowski T, Demoule A: Prevalence and prognosis impact of patient–ventilator asynchrony in early phase of weaning according to two detection methods. ANESTHESIOLOGY 2017; 127:989–97
2. Demoule A, Clavel M, Rolland-Debord C, Perbet S, Terzi N, Kouatchet A, Wallet F, Roze H, Vargas F, Guerin C, Dellamonica J, Jaber S, Brochard L, Similowski T: Neurally adjusted ventilatory assist as an alternative to pressure support ventilation in adults: A French multicentre randomized trial. Intensive Care Med 2016; 42:1723–32
3. Blanch L, Villagra A, Sales B, Montanya J, Lucangelo U, Luján M, García-Esquirol O, Chacón E, Estruga A, Oliva JC, Hernández-Abadia A, Albaiceta GM, Fernández-Mondejar E, Fernández R, Lopez-Aguilar J, Villar J, Murias G, Kacmarek RM: Asynchronies during mechanical ventilation are associated with mortality. Intensive Care Med 2015; 41:633–41
4. Vaporidi K, Babalis D, Chytas A, Lilitsis E, Kondili E, Amargianitakis V, Chouvarda I, Maglaveras N, Georgopoulos D: Clusters of ineffective efforts during mechanical ventilation: Impact on outcome. Intensive Care Med 2017; 43:184–91
5. de Wit M, Miller KB, Green DA, Ostman HE, Gennings C, Epstein SK: Ineffective triggering predicts increased

Downloaded from anesthesiology.pubs.asahq.org by guest on 04/03/2020
Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.

duration of mechanical ventilation. Crit Care Med 2009; 37:2740–5

6. Colombo D, Cammarota G, Alemani M, Carenzo L, Barra FL, Vaschetto R, Slutsky AS, Della Corte F, Navalesi P: Efficacy of ventilator waveforms observation in detecting patient-ventilator asynchrony. Crit Care Med 2011; 39:2452–7
7. Goligher EC, Ferguson ND, Brochard LJ: Clinical challenges in mechanical ventilation. Lancet 2016; 387(North American Edition):1856–66
8. Thille AW, Cabello B, Galia F, Lyazidi A, Brochard L: Reduction of patient-ventilator asynchrony by reducing tidal volume during pressure-support ventilation. Intensive Care Med 2008; 34:1477–86
9. Beitler JR, Sands SA, Loring SH, Owens RL, Malhotra A, Spragg RG, Matthay MA, Thompson BT, Talmor D: Quantifying unintended exposure to high tidal volumes from breath stacking dyssynchrony in ARDS: The BREATHE criteria. Intensive Care Med 2016; 42:1427–36
10. Ranieri VM, Rubenfeld GD, Thompson BT, Ferguson ND, Caldwell E, Fan E, Camporota L, Slutsky AS; ARDS Definition Task Force: Acute respiratory distress syndrome: The Berlin Definition. JAMA 2012; 307:2526–33
11. Papazian L, Forel JM, Gacouin A, Penot-Ragon C, Perrin G, Loundou A, Jaber S, Arnal JM, Perez D, Seghboyan JM, Constantin JM, Courant P, Lefrant JY, Guérin C, Prat G, Morange S, Roch A; ACURASYS Study Investigators: Neuromuscular blockers in early acute respiratory distress syndrome. N Engl J Med 2010; 363:1107–16
12. Schmidt M, Banzett RB, Raux M, Morélot-Panzini C, Dangers L, Similowski T, Demoule A: Unrecognized suffering in the ICU: Addressing dyspnea in mechanically ventilated patients. Intensive Care Med 2014; 40:1–10

Downloaded from anesthesiology.pubs.asahq.org by guest on 04/03/2020
Copyright © 2017, the American Society of Anesthesiologists, Inc. Wolters Kluwer Health, Inc. Unauthorized reproduction of this article is prohibited.